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=> s pertactin
L1           60 FILE HCAPLUS
L2           99 FILE MEDLINE
L3          101 FILE BIOSIS

TOTAL FOR ALL FILES
L4          260 PERTACTIN

=> s l4 and agglut?
L5           42 FILE HCAPLUS
L6           21 FILE MEDLINE
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L7          20 FILE BIOSIS

TOTAL FOR ALL FILES
L8          83 L4 AND AGGLUT?

=> s l8 and tox?
L9          22 FILE HCAPLUS
L10         19 FILE MEDLINE
L11         17 FILE BIOSIS

TOTAL FOR ALL FILES
L12         58 L8 AND TOX?

=> s l12 and pertus?
L13         21 FILE HCAPLUS
L14         19 FILE MEDLINE
L15         17 FILE BIOSIS

TOTAL FOR ALL FILES
L16         57 L12 AND PERTUS?

=> s l16 and (hemag? or haemag?)
L17         14 FILE HCAPLUS
L18         19 FILE MEDLINE
L19         17 FILE BIOSIS

TOTAL FOR ALL FILES
L20         50 L16 AND (HEMAG? OR HAEMAG?)

=> s l20 and vaccin?
L21         10 FILE HCAPLUS
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L23         15 FILE BIOSIS

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L24         42 L20 AND VACCIN?

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=> s l24
L25         10 FILE HCAPLUS
L26         17 FILE MEDLINE
L27         15 FILE BIOSIS
L28          2 FILE USPATFULL

TOTAL FOR ALL FILES
L29         44 L24
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=> dup rem l29
PROCESSING COMPLETED FOR L29
L30 30 DUP REM L29 (14 DUPLICATES REMOVED)

=> d bib ab 1-

L30 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:761878 HCAPLUS
DN 126:37038
TI Acellular **pertussis vaccines** and methods of preparation thereof
IN Vose, John R.; Fahim, Raafat E. F.; Jackson, Gail E. D.; Tan, Larry U. L.; Herbert, Andrew; Boux, Leslie; Barreto, Luis; Thipphawong, John; Klein, Michel H.
PA Connaught Laboratories Limited, Can.; Vose, John R.; Fahim, Raafat E. F.; Jackson, Gail E. D.; Tan, Larry U. L.; Herbert, Andrew; Boux, Leslie; Barreto, Luis; Thipphawong, John; Klein, Michel H.
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
PI WO 9634623 A1 961107
DS W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 96-CA278 960502
PRAI US 95-433646 950504
US 95-501743 950712
DT Patent
LA English
AB Acellular **pertussis vaccines** comprise purified **toxin** or **toxoid** thereof, filamentous **hemagglutinin**, **pertactin** and fimbrial **agglutinogens** formulated to confer protection to at least 70% of members of an at-risk population. The fimbrial **agglutinogens** may be prepd. from a Bordetella strain, particularly a B. **pertussis** strain, by a multiple step procedure involving extn. of the fimbrial **agglutinogens** from cell paste and concg. and purifying the extd. material.

L30 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:606393 HCAPLUS
DN 125:245151
TI **Pertussis**-specific cell-mediated immunity in infants after **vaccination** with a tricomponent acellular **pertussis vaccine**
AU Zepp, F.; Knuf, M.; Habermehl, P.; Schmitt, H. J.; Rebsch, C.; Schmidtke, P.; Clemens, R.; Slaoui, M.
CS Pediatric Immunology Infectious Diseases, Children's Hospital, Johannes Gutenberg University Mainz, Mainz, D-55101, Germany
SO Infect. Immun. (1996), 64(10), 4078-4084
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB The aim here was to investigate **pertussis**-specific cell-mediated immunity in infants **vaccinated** with a tricomponent acellular **vaccine**. Infants were investigated

during a primary **vaccination** schedule from the 3rd month of life to the 6th month as well as before and after a booster at 15-24 mo. This is the first report of specific cell-mediated immune responses to **pertussis**-related antigens in infants below the age of 12 mo. The data show that the **vaccine** induces T-cell responses specific for the **vaccine** components, detoxified **pertussis toxin**, filamentous **hemagglutinin**, and **pertactin**, that increase progressively over the course of the **vaccination** schedule. In contrast to declining antibody titers, cell-mediated immune responses are stable over the post-primary to pre-booster period. **Vaccination** results in a progressive increase in the no. of T cells that express activation marker CD45RO preferentially on CD4-pos. T cells after stimulation with **pertussis** antigens. Measurements of cytokine secretion profiles demonstrated a preferential induction of interleukin 2- and .gamma. interferon-producing T-helper 1 cells and only low prodn. of interleukin 10. The obsd. persistence of the specific cell-mediated immunity may have a bearing on the protective mechanisms induced by **pertussis vaccination**.

L30 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:735791 HCAPLUS
DN 126:88024
TI Collaborative study for the evaluation of enzyme-linked immunosorbent assays used to measure human antibodies to Bordetella **pertussis** antigens
AU Lynn, Freyja; Reed, George F.; Meade, Bruce D.
CS Food and Drug Administration, Center Biologics Evaluation and Research, Rockville, MD, 20852, USA
SO Clin. Diagn. Lab. Immunol. (1996), 3(6), 689-700
CODEN: CDIMEN; ISSN: 1071-412X
DT Journal
LA English
AB Acellular **pertussis vaccines** are being evaluated in multiple clin. studies, and human immunogenicity data will likely be pivotal in the appraisal of **vaccine** responses between populations and the responses to different **vaccine** combinations. Antibody response to **pertussis** antigens is also used in the diagnosis of **pertussis**. An international study was designed to assess the comparability of data generated in different labs. by enzyme-linked immunosorbent assays (ELISAs). Thirty-three participating labs. were asked to quantitate specific antibody to **pertussis toxin** (PT), filamentous **hemagglutinin** (FHA), **pertactin** (PRN), or fimbrial proteins (FIM) in 21 samples. Samples were to be assayed in triplicate in five independent assays by each ELISA routinely performed in the lab. to assess intra-assay, interassay, and population variability. The mean sample values were used to compare quant. results among the labs. Thirteen of the 32 labs. which submitted evaluable data for an assay to measure antibodies to PT, 12 of 30 labs. with assays for FHA, 10 of 17 labs. with assays for PRN, and 6 of 13 labs. with assays for FIM maintained a coeff. of variation below 20% for 75% of the samples tested. Assays that measure antibodies to FIM appear to be less precise than the other assays. Precision varied among labs. that used similar methods. The relative values of intra- and interassay variabilities were not consistent for a given assay within a lab., indicating that the sources of these variability components may be unrelated. Precision

and agreement appeared less reliable for samples with low antibody levels. Ranking and regression analyses suggest that some labs. generated comparable quant. results, although direct comparison or combination of results from different labs. remains difficult to support. Calibration to the U.S. Ref. **Pertussis** Antisera appears to have been successful at standardizing the results in some labs. Statistical analyses are affected by assay precision and are not necessarily reliable sole predictors of biol. relevant differences in quant. results. If results from different labs. must be compared, appropriate studies of precision and quant. agreement should be conducted to support the specific comparisons.

L30 ANSWER 4 OF 30 MEDLINE DUPLICATE 1
AN 96221456 MEDLINE
TI **Pertussis vaccines**: acellular versus whole-cell.
AU Boughton C R
CS Department of Infectious Diseases, Prince Henry Hospital, Sydney, NSW.
SO MEDICAL JOURNAL OF AUSTRALIA, (1996 May 6) 164 (9) 564-6.
Journal code: M26. ISSN: 0025-729X.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9609
AB Acellular **pertussis vaccines** containing purified Bordetella **pertussis** antigens have now been extensively field tested. They produce a significantly lower rate of reactions than whole-cell **vaccines** and their efficacy is either comparable or superior. At least three antigens appear necessary for good protection: **pertussis toxoid**, filamentous **haemagglutinin** and **pertactin** (an outer-membrane protein); fimbrial **agglutinogens** are probably not needed. It is hoped that a cellular **pertussis vaccine** will soon be licensed in Australia for both primary and booster **vaccination**.

L30 ANSWER 5 OF 30 BIOSIS COPYRIGHT 1997 BIOSIS
AN 96:337853 BIOSIS
DN 99060209
TI Antibody response and reactions to completion of a four-dose series with a two- or three-component acellular **pertussis vaccine** compared to whole cell **pertussis vaccine**.
AU Pichichero M E; Green J L; Francis A B; Marsocci S M; Murphy A M L; Buscarino C
CS Dep. Microbiol. Immunol., Univ. Rochester Med. Cent., 601 Elmwood Ave., Box 672, Rochester, NY 14642, USA
SO Scandinavian Journal of Infectious Diseases 28 (2). 1996. 159-163.
ISSN: 0036-5548
LA English
AB We compared the reactions and immunogenicity of DT acellular **pertussis** (DTaP) **vaccines** containing **pertussis toxoid** (PT) and filamentous **haemagglutinin** (FHA) (2-component DTaP) or PT, FHA and **pertactin** (PRN) (3-component DTaP **vaccine**) with a whole cell (DTwP) **vaccine** as a fourth-dose booster in 158 children (15-20 months old) who had received 3 primary **vaccine** doses with the same **vaccines** at 2, 4 and 6

months of age. Randomization was 3:1 for DTaP: DTwP and all children received concomitant oral polio **vaccine** (OPV). Fever (gt 38 degree C), irritability, local injection site erythema (gt 10 mm), swelling (gt 10 mm), and pain (moderate or more) were assessed for 72 h after booster **vaccination**. DTwP **vaccinees** had a higher incidence of fever (29.4%) and injection-site pain (45.7%) than 3-component DTaP **vaccinees** (fever, 9.6%, p lt 0.02; injection-site pain, 3.8%, p lt 0.01); 2-component DTaP **vaccinees** had less injection-site pain (8.3%, p lt 0.01). Pre- and post-**vaccination** immunoglobulin G (IgG) antibody was measured by enzyme-linked immunosorbent assay (ELISA). Pre- and post anti-PT levels were similar for all 3 **vaccine** groups. Anti-FHA antibody was higher pre- and post-**vaccination** for both DTaP **vaccine** groups compared with the DTwP **vaccinees** (p lt 0.01 for all comparisons). For 3-component DTaP **vaccinees**, anti-PRN antibody was higher pre- and post-**vaccination** compared to DTwP **vaccinees** (p lt 0.01 for both comparisons). Tetanus antibody was higher pre- and post-**vaccination** for DTwP versus both DTaP **vaccine** groups, and diphtheria antibody was similar pre- and post-**vaccination** for all 3 groups. These 2- and 3-component DTaP **vaccines** produce less common reactions and comparable or higher antibody to the components they contain (except tetanus) than DTwP **vaccine** when given as a booster to 15- to 20-month-old children previously primed with the same **vaccine**.

L30 ANSWER 6 OF 30 MEDLINE DUPLICATE 2
AN 96366334 MEDLINE
TI Long-term human serum antibody responses after immunization with whole-cell **pertussis vaccine** in France.
AU Grimprel E; Begue P; Anjak I; Njamkepo E; Francois P; Guiso N
CS Hopital d'enfants Armand-Trousseau, Paris, France.
SO CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (1996 Jan) 3 (1) 93-7.
Journal code: CB7. ISSN: 1071-412X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9612
AB Three hundred sixty children were tested for **pertussis** serology 0.5 to 1.58 months after complete whole-cell **pertussis vaccination**. An immunoblot assay was used to detect serum antibodies to **pertussis toxin**, filamentous **hemagglutinin**, adenylate cyclase-hemolysin, and **pertactin**, and **agglutination** was used for detection of anti-**agglutinogen** antibodies. Antibodies against **pertussis toxin**, **pertactin**, and **agglutinogens** decreased rapidly after **vaccination** but increased secondarily, suggesting exposure to infected persons. In contrast, anti-filamentous **hemagglutinin** antibodies persisted and anti-adenylate cyclase-hemolysin antibodies increased continuously, suggesting either cross-reaction with non-Bordetella antigens or exposure to Bordetella isolates expressing these two antigens, including Bordetella **pertussis**. These data suggest that unrecognized **pertussis** is common in France despite massive and sustained immunization in infants and that **vaccinated** children become susceptible to infection more than 6 years after their last

vaccination.

L30 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1996:147750 HCAPLUS
DN 124:200276
TI Separating protective components of Bordetella **pertussis**
IN Suehara, Akihiro; Yamamoto, Eiji; Fujii, Shigeo
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
PI WO 9529934 A1 951109
DS W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-JP830 950426
PRAI JP 94-91565 940428
DT Patent
LA English
AB A method of efficiently sepg. protective components of B. **pertussis** is disclosed. On the basis of differences in adsorbability to Ca phosphate gel formed by adding Ca2+ to a B. **pertussis** culture in the presence of excess phosphate ions, protective components of B. **pertussis** are sepd. from the B. **pertussis** culture. Traditionally, protective components of B. **pertussis** have been sepd. using different methods for the resp. components. According to the present invention, the use of the same means of purifn. for all subject components makes it possible to purify each component with high efficiency and high recovery rate, an aspect very advantageous for industrial prodn. It is also possible to efficiently produce an improved purified **pertussis** component **vaccine** comprising an effective combination of **pertussis** filamentous **hemagglutinin** (FHA), **pertactin** (PRN, 69K-OMP), **pertussis** fimbriae (FIM), and **pertussis** **toxin** (PT).

L30 ANSWER 8 OF 30 USPATFULL
AN 95:76066 USPATFULL
TI Purification of a **pertussis** outer membrane protein
IN Jackson, Gail, Richmond Hill, Canada
Fahim, Raafat, Mississauga, Canada
Tan, Larry, Mississauga, Canada
Chong, Pele, Thornhill, Canada
Vose, John, Aurora, Canada
Klein, Michel, Willowdale, Canada
PA Connaught Laboratories Limited, Willowdale, Canada (non-U.S. corporation)
PI US 5444159 950822
AI US 92-930595 921106 (7)
PRAI GB 90-7657 900404
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Krsek-Staples, Julie
LREP Sim & McBurney
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 614
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Pertactin** (formerly 69 kDa protein) is recovered in stable biologically pure form having no detectable adenylate cyclase activity from fermentation broth from the fermentation of Bordetella **pertussis** as well as from the cells. The broth is processed to selectively remove **pertussis toxin** (PT) and filamentous **haemagglutinin** (FHA), the **pertactin** is precipitated by ammonium sulphate and the precipitate is dissolved in buffer at pH 6.0 to 8.5, the solution then is passed through hydroxyapatite and ion-exchange chromatograph columns before final ultrafiltration. Cells are extracted with urea and the extract ultrafiltered and diafiltered. The **pertactin** is precipitated from the extract and the precipitate processed as above. In a variation, the broth is contacted with ammonium sulphate to precipitate **pertactin**, PT and FHA, the precipitate is dissolved and the PT and FHA selectively removed, before the solution is passed to the chromatograph columns.

L30 ANSWER 9 OF 30 USPATFULL
AN 95:71262 USPATFULL
TI Manipulation of gene copy number in bordetella
IN Loosmore, Sheena, Aurora, Canada
Zealey, Gavin, Thornhill, Canada
Yacoob, Reza, Mississauga, Canada
Klein, Michel, Willowdale, Canada
PA Connaught Laboratories Limited, Willowdale, Canada (non-U.S. corporation)
PI US 5439810 950808
AI US 92-911291 920709 (7)
PRAI GB 91-15332 910716
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Tuscan, Michael
LREP Sim & McBurney
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 908
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Protein expression levels from Bordetella strains, particularly Bordetella **pertussis**, are altered by genetic modification to a natural Bordetella strain whereby one or more of the natural genes, particularly including the **TOX**, FHA, CYA and PRN genes, is deleted from the genome of the natural strain and one or more of the natural genes or a genetic mutation thereof, particularly a genetically-detoxified **TOX*** gene, or a hybrid gene, is inserted into the genome of the natural strain to provide at least two copies of one or more of the natural genes or genetic mutation thereof or hybrid gene, singly or in tandem. The altered genotype Bordetella strain is useful in producing whole-cell or defined component **vaccines** against Bordetella, particularly whooping cough, which may be employed in combination with other **vaccines**.

L30 ANSWER 10 OF 30 MEDLINE
AN 96126006 MEDLINE
TI Household contact study of Bordetella **pertussis**

infections.
AU Deen J L; Mink C A; Cherry J D; Christenson P D; Pineda E F; Lewis K; Blumberg D A; Ross L A
CS Department of Pediatrics, UCLA Medical Center, USA.
NC 1-A115124
SO CLINICAL INFECTIOUS DISEASES, (1995 Nov) 21 (5) 1211-9.
Journal code: A4J. ISSN: 1058-4838.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9605
AB Household contacts of primary **pertussis** cases were evaluated. Infection was determined by culture, direct fluorescent antibody assay, and serological criteria. **Agglutinin** titers and values of ELISA IgG and IgA antibodies to lymphocytosis-promoting factor, filamentous **hemagglutinin**, and **pertactin** were determined. In 39 households 255 subjects were exposed; 114 remained well (group 1), 53 had mild illness (group 2), and 88 had **pertussis** (group 3). The infection rates were 46% (group 1), 43% (group 2), and 80% (group 3). In a subgroup of subjects seen within 14-28 days of exposure, it was found that none with clinical **pertussis** had a value of IgG antibody to **pertactin** in acute-phase sera of > or = 50 ELISA units (EU) per mL or an **agglutinin** titer of > 256. Of the primary cases, 53% were > or = 13 years of age. These data point out the importance of Bordetella **pertussis** infections in adolescents and adults as a source of infection in young children. Our subgroup data suggest that high values of antibody to **pertactin** and high **agglutinin** titers may be predictive of protection against clinical **pertussis**
.

L30 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1995:467421 HCAPLUS
DN 122:222580
TI Adjuvanticity and protective immunity elicited by Bordetella **pertussis** antigens encapsulated in poly(DL-lactide-co-glycolide) microspheres
AU Shahin, Roberta; Leef, Mary; Eldridge, John; Hudson, Michael; Gilley, Richard
CS Lab. Pertussis, Cent. Biol. Eval., Bethesda, MD, USA
SO Infect. Immun. (1995), 63(4), 1195-200
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Purified Bordetella **pertussis** antigens, encapsulated in biodegradable poly(DL-lactide-co-glycolide) (DL-PLG) microspheres, were evaluated for their immunogenicity and ability to elicit a protective immune response against B. **pertussis** respiratory infection. Microencapsulated **pertussis toxoid**, filamentous **hemagglutinin**, and **pertactin** all retained their immunogenicity when administered parenterally. Intranasal immunization with a low dose (1 .mu.g) of encapsulated filamentous **hemagglutinin**, **pertussis toxoid**, or **pertactin** elicited strong specific IgG and IgA antibody responses in respiratory secretions that were greater in magnitude than the responses elicited by the same doses of unencapsulated antigen. Intranasal

immunization with as little as 1 .mu.g of encapsulated **pertussis** antigen prior to infection reduced the bacterial recovery by 3 log130 CFU. However, intranasal immunization with the same low doses of unencapsulated antigens did not reduce infection. Intranasal administration of a combination of 1 .mu.g of ech of the microencapsulated **pertussis** antigens was more effective in reducing bacterial infection than administration of any single microencapsulated antigen. Intranasal administration of microencapsulated B. **pertussis** antigens elicits high levels of specific antibody coinciding with protection against infection when these microspheres are administered to the respiratory tract. These data provide evidence of the respiratory adjuvanticity of three different DL-PLG microsphere prepns., each of which contains a unique b. **pertussis** antigen.

L30 ANSWER 12 OF 30 MEDLINE DUPLICATE 3
AN 95388474 MEDLINE
TI Relationships between functional assays and enzyme immunoassays as measurements of responses to acellular and whole-cell **pertussis vaccines**.
AU Meade B D; Lynn F; Reed G F; Mink C M; Romani T A; Deforest A; Deloria M A
CS Division of Bacterial Products, Food and Drug Administration, Rockville, MD 20852-1448, USA..
NC N01-AI72629 (NIAID)
N01-AI25135 (NIAID)
N01-AI62515 (NIAID)
+
SO PEDIATRICS, (1995 Sep) 96 (3 Pt 2) 595-600.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9512
AB OBJECTIVE. To examine the relationships between functional assays and antigen-specific enzyme immunoassays in sera from a multicenter trial of 13 different experimental acellular **pertussis vaccines** and 2 licensed whole-cell **vaccines**, and to determine whether correlations previously observed among assays of specimens from **pertussis** patients and whole-cell **vaccinees** would apply to specimens from infants immunized with purified components in acellular **vaccines**. METHODS. Postimmunization sera were assayed for immunoglobulin G antibodies to **pertussis toxin** (PT), filamentous **hemagglutinin**, **pertactin** (PRN), and a mixture of types 2 and 3 fimbriae (FIM) by enzyme-linked immunosorbent assay, for whole-cell **agglutinins** (AGGs) and for PT-neutralizing antibodies by the Chinese hamster ovary (CHO) cell assay. Assay results were compared for individual sera, as well as for geometric mean antibody concentrations or titers (GMTs) calculated by **vaccine** or overall. RESULTS. For the 15 **vaccines**, the PT GMTs were highly correlated with the CHO assay GMTs (r = .92), and the FIM GMTs were highly correlated with the AGG GMTs (r = .96). For individual postvaccination sera, there was a significant correlation between the CHO titers and levels of antibody to PT

whether the 15 **vaccines** were considered separately (.59 < or = r < or = .85) or combined (r = .81). For individual sera from infants immunized with the two whole-cell **vaccines** or any of the four acellular **vaccines** containing FIM, a strong correlation between AGG titer and FIM antibody was observed whether the **vaccines** were considered separately (.83 < or = r < or = .91) or together (r = .86). One **vaccine** without detectable FIM produced a measurable AGG response; for this **vaccine**, a moderate but significant correlation (R = .58) between PRN antibody and AGG titer was observed. CONCLUSION. These data indicate that appropriate antigen-specific enzyme-linked immunosorbent assays will furnish results similar to those provided by the CHO and AGG assays in the evaluation of the immunogenicity of component **vaccines**. Antibodies to FIM seem to include the most important AGGs; however, there is evidence that **agglutination** by PRN antibody may be detected in the absence of antibody to FIM.

L30 ANSWER 13 OF 30 MEDLINE DUPLICATE 4
AN 95388471 MEDLINE
TI Effect of gender, race, and parental education on immunogenicity and reported reactogenicity of acellular and whole-cell **pertussis vaccines**.
AU Christy C; Pichichero M E; Reed G F; Decker M D; Anderson E L; Rennels M B; Englund J A; Edwards K M; Steinhoff M C
CS Department of Pediatrics, University of Rochester School of Medicine, NY, USA..
NC N01-AI72629 (NIAID)
N01-AI25135 (NIAID)
N01-AI62515 (NIAID)
SO PEDIATRICS, (1995 Sep) 96 (3 Pt 2) 584-7.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9512
AB OBJECTIVE. To determine whether gender, race (black or white), or level of parental education influenced serologic responses or reporting of clinical reactions after immunization with acellular (DTaP) or whole-cell (DTP) **pertussis vaccine** with diphtheria and tetanus **toxoids** combined. METHODS. Healthy infants were prospectively randomized to receive one of 13 DTaP, Lederle DTP, or another DTP. Parents recorded the occurrence of adverse reactions for 2 weeks after each inoculation. Sera obtained before the first immunization and 1 month after the third immunization were analyzed for antibody to **pertussis toxin**, filamentous **hemagglutinin**, fimbriae, and **pertactin** (PRN). Chinese hamster ovary cell **pertussis toxin** neutralization assays were performed, and levels of **agglutinating** antibodies determined. RESULTS. Prevaccination antibody levels did not differ by race, gender, or parental education. Postimmunization geometric mean titers (GMTs) were strongly and consistently associated with race. For both DTaP and DTP and for every included antigen, postimmunization GMTs were about twice as high for black as for

white infants. Among DTaP recipients, these differences were significant for **pertussis toxin**, Chinese hamster ovary cell **pertussis toxin** neutralization assay, filamentous **hemagglutinin**, PRN, and **agglutinins**; among the much smaller sample of WCL recipients, the differences achieved or approached statistical significance for **agglutinins**, PRN, and fimbriae. These findings were confirmed by regression analyses that controlled for gender, parental education, study site, and preimmunization antibody level. Reported reactions were not correlated with parental education level and showed no material correlation with gender. Black infants were reported to have had more pain than white infants after receiving WCL and DTaP and were reported to be more fussy after receiving WCL. CONCLUSIONS. The consistently higher postimmunization GMTs among black infants seems to be a real finding for which we have no explanation; the infants did not significantly differ by race in **vaccine** assignment, preimmunization antibody levels, age at immunization, or interval from immunization to phlebotomy. These observations should be confirmed and further evaluated in future **pertussis vaccine** trials. Reported differences by race in pain and fussiness after receiving WCL might reflect chance, differences by race in the occurrence of reactions, or differences by race in the reporting of reactions.

L30 ANSWER 14 OF 30 MEDLINE DUPLICATE 5
AN 95388468 MEDLINE
TI Description and evaluation of serologic assays used in a multicenter trial of acellular **pertussis vaccines**.
AU Meade B D; Deforest A; Edwards K M; Romani T A; Lynn F; O'Brien C H; Swartz C B; Reed G F; Deloria M A
CS Division of Bacterial Products, Food and Drug Administration, Rockville, MD 20852-1448, USA..
NC N01 AI72629 (NIAID)
N01 AI25135 (NIAID)
N01 AI62515 (NIAID)
+
SO PEDIATRICS, (1995 Sep) 96 (3 Pt 2) 570-5.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9512
AB OBJECTIVE. To describe and evaluate the assays used to measure the antibody responses in infants to 13 experimental acellular **pertussis vaccines** and 2 licensed whole-cell **pertussis vaccines**. METHODS. During a 53-week period, preimmunization and postimmunization sera were assayed for immunoglobulin G antibodies to **pertussis toxin**, filamentous **hemagglutinin**, **pertactin**, and a mixture of type 2 and type 3 fimbriae by enzyme-linked immunosorbent assay (ELISA), for whole-cell **agglutinins** (AGG), and for **pertussis toxin**-neutralizing antibodies by the Chinese hamster ovary cell assay. All ELISA reagents were characterized to assure antigen and isotype specificity of the assays. Intralaboratory reproducibility and temporal stability were evaluated by analysis of results of control sera and by assessment

of the response to the control whole-cell **vaccine**. Interlaboratory reproducibility was assessed by repeating the assays on preimmunization and postimmunization sera for 10% of the infants in a second laboratory. RESULTS. For control sera having antibody concentrations at least four times the minimum level of detection, the coefficients of variation within and between the ELISAs consistently were less than 20%. Trend analysis indicated that none of the assays drifted by more than 20% during the study period, and no significant drift was seen in the response to the control whole-cell **vaccine**. Results from the two laboratories correlated well; correlation coefficients were .93 or greater for the four ELISAs, .79 for the Chinese hamster ovary cell assay, and .82 for the AGG assay. For four of the six assays, there was either no difference or a modest (< 15%) difference in the geometric mean values for sera tested in both laboratories. Larger quantitative differences were observed for the AGG (45% difference) and **pertactin** (61% difference) assays. CONCLUSION. Assay reproducibility and stability indicate that the standardized methods can be transferred between laboratories, and that the results accrued during a 1-year period for the 15 **vaccines** can be compared.

L30 ANSWER 15 OF 30 MEDLINE DUPLICATE 6
AN 95388467 MEDLINE
TI A randomized comparison of reactogenicity and immunogenicity of two whole-cell **pertussis vaccines**.
AU Steinhoff M C; Reed G F; Decker M D; Edwards K M; Englund J A; Pichichero M E; Rennels M B; Anderson E L; Deloria M A; Meade B D
CS Department of International Health, School of Medicine, Johns Hopkins University, Baltimore, MD 21205, USA..
NC N01 AI72629 (NIAID)
N01 AI25135 (NIAID)
N01 AI62515 (NIAID)
+
SO PEDIATRICS, (1995 Sep) 96 (3 Pt 2) 567-70.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9512
AB OBJECTIVE. To compare prospectively the reactogenicity and immunogenicity of two licensed whole-cell **pertussis vaccines**. METHODS. We conducted a prospective, randomized, double-blinded assessment of two licensed whole-cell **pertussis vaccines** with diphtheria and tetanus **toxoids** that were included in a multicenter trial evaluating 13 acellular **pertussis vaccines**. Infants were immunized at 2, 4, and 6 months of age with a single lot of Lederle (309 infants) or Massachusetts Public Health Biologic Laboratories (MPHBL; 94 infants) **vaccine**. RESULTS. The group receiving the Lederle **vaccine** demonstrated significantly higher antibody titers to **pertussis toxin** by enzyme-linked immunosorbent assay (ELISA) and by the Chinese hamster ovary cell **pertussis toxin** neutralization assay, and to fimbrial antigens by ELISA, as well as higher mean

agglutinin titers. In contrast, the group receiving the MPHBL **vaccine** demonstrated higher ELISA antibody levels to filamentous **hemagglutinin** and **pertactin**. Similar differences were observed in the proportions of **vaccinees** seroconverting to these antigens. Rates of systemic and local reactions were relatively low for both **vaccines**. Although the Lederle product had substantially lower reactogenicity in this study than previously reported for that **vaccine**, the MPHBL **vaccine** was significantly less reactogenic in nearly all clinical categories. CONCLUSION. The two whole-cell **vaccines** demonstrated statistically significant differences in postimmunization antibody levels to all six evaluated **pertussis** antigens. Whether these statistically significant differences in antibody levels have clinical relevance is not clear. Rates of nearly all local and systemic reactions were significantly lower among the MPHBL group than the Lederle group. Licensed whole-cell diphtheria-tetanus-**pertussis vaccines** produced by different manufacturers cannot be assumed to be similar in reactogenicity or immunogenicity.

L30 ANSWER 16 OF 30 MEDLINE DUPLICATE 7
AN 95388465 MEDLINE
TI Comparison of 13 acellular **pertussis vaccines**: overview and serologic response [see comments].
CM Comment in: Pediatrics 1996 Oct;98(4 Pt 1):800
AU Edwards K M; Meade B D; Decker M D; Reed G F; Rennels M B; Steinhoff M C; Anderson E L; Englund J A; Pichichero M E; Deloria M A
CS Department of Pediatrics, Food and Drug Administration, Rockville, MD, USA.
NC N01-AI25135 (NIAID)
N01-AI62515 (NIAID)
N01-AI72629 (NIAID)
+
SO PEDIATRICS, (1995 Sep) 96 (3 Pt 2) 548-57.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9512
AB OBJECTIVE. To compare the immunogenicity of a licensed conventional whole-cell (WCL) and 13 diphtheria-tetanus-acellular **pertussis** (DTaP) **vaccines** that differed in source, method of manufacture, and included antigens; all **vaccines** included diphtheria and tetanus **toxoids**. METHODS. Healthy infants were enrolled through six university-based **vaccine** and treatment evaluation units and were randomized to receive one of the study **vaccines** at 2, 4, and 6 months of age. Sera were obtained before the first immunization and 1 month after the third immunization and were analyzed for antibody to **pertussis toxin** (PT), filamentous **hemagglutinin**, fimbriae, **pertactin**, and diphtheria and tetanus **toxins**. Chinese hamster ovary cell **toxin** neutralization assays were performed, and levels of **agglutinating** antibodies were determined. RESULTS. Of 2342 infants enrolled, 1942 contributed usable preimmunization and postimmunization serum specimens. Each

vaccine produced significant increases in antibodies directed against the included antigens; postimmunization antibody titers differed significantly among the DTaP **vaccines**. For each evaluated antigen, the majority of DTaP **vaccines** produced antibody responses that equaled or exceeded those produced by WCL. For some antigens (eg, PT), mean antibody levels by **vaccine** correlated poorly with the quantity of antigen included in each **vaccine**; for others (eg., fimbriae), there was a close correlation. CONCLUSION. Although serologic correlates of **pertussis** immunity are not defined, it is clear that DTaP **vaccines** can stimulate immune responses that exceed those of licensed whole-cell **vaccine** with respect to the measured antibodies. Particularly for PT, immunogenicity seems to depend on factors in addition to antigen concentration, possibly including antigen derivation and formulation. No DTaP was most or least immunogenic with respect to all included antigens.

L30 ANSWER 17 OF 30 MEDLINE DUPLICATE 8

AN 95278276 MEDLINE

TI Immunogenicity and safety of a monovalent, multicomponent acellular **pertussis vaccine** in 15 month-6-year-old German children. Monovalent Acellular **Pertussis Vaccine** Study Group.

AU Stehr K; Heininger U; Uhlenbusch R; Angersbach P; Hackell J; Eckhardt T

CS Universitatsklinik mit Poliklinik fur Kinder und Jugendliche, Erlangen, Germany.

SO EUROPEAN JOURNAL OF PEDIATRICS, (1995 Mar) 154 (3) 209-14. Journal code: END. ISSN: 0340-6199.

CY GERMANY: Germany, Federal Republic of

DT (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY)

LA English

FS Priority Journals

EM 9509

AB Immunization against **pertussis** has been re-recommended for healthy children in Germany in 1991. In addition the former restriction of immunizing only in the first 2 years of life was abolished. In children born before 1991 immunization rates against **pertussis** were 15% or less. With the new recommendations physicians are now faced with an increasing demand of parents for catch-up **vaccinations** in these children. Since they were immunized against diphtheria and tetanus previously monovalent **pertussis vaccines** are needed for this indication. Therefore a monovalent, multicomponent acellular **pertussis vaccine** was studied in 249 German children 15 months to 6 years of age. Three doses were administered at 6-10 week intervals. Reactogenicity and antibody responses against the **vaccine** antigens **pertussis toxin** (PT), filamentous **haemagglutinin** (FHA), 69-kd antigen (**pertactin**) and fimbriae-2 (**agglutinogen**) were investigated. Local and systemic reactions were minimal in frequency and severity. Antibody responses against all **vaccine** antigens were pronounced with 93%-100% of **vaccinees** demonstrating at least four fold titre rises above pre-immunization after the third dose. These findings indicate that this monovalent, multicomponent acellular **pertussis vaccine** with excellent immunogenicity

and low reactogenicity is an appropriate candidate for closing immunization gaps in older children in countries with previously low **vaccination** rates against **pertussis**. Based on the results of this study the monovalent acellular **pertussis vaccine** was licensed in Germany in January 1994.

L30 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 1997 ACS DUPLICATE 9
AN 1995:267973 HCAPLUS
DN 122:53481
TI Immunoelectron microscopy of antigens of Bordetella **pertussis** using monoclonal antibodies to **agglutinogens** 2 and 3, filamentous **hemagglutinin**, **pertussis toxin**, **pertactin** and adenylate cyclase **toxin**
AU Blom, Jens; Heron, Iver; Hendley, J. Owen
CS Department of Molecular Cell Biology, Statens Seruminstitut, Copenhagen, DK-2300, Den.
SO APMIS (1994), 102(9), 681-9
CODEN: APMSEL; ISSN: 0903-4641
DT Journal
LA English
AB Immunogold electron microscopy and monoclonal antibodies (Mabs) were used to localize surface-related antigens of Bordetella **pertussis**. Unfixed organisms of B. **pertussis** strains which are included in the Danish whole-cell **pertussis vaccine** and fixed cells from a vial of **vaccine** were examd. Mabs to **agglutinogens** 2 and 3 labeled fimbria-like structures on both live and fixed cells in a serotype-specific manner. Mab against **pertactin**, a 69 kDa outer membrane protein, produced intense labeling of the surface of unfixed cells, whereas staining was reduced when fixed cells were examd. Mabs against filamentous **hemagglutinin** (FHA) stained aggregates of material between or adherent to both live and fixed cells. Negligible labeling of FHA on cell surfaces was obsd. Mabs to **pertussis toxin** and adenylate cyclase **toxin** labeled loose-structured material which was adherent to or between cells, but neither of these **toxin** antigens was expressed on the surface of B. **pertussis** in Mab recognizable form. It is therefore suggested that these antigens are readily dispersed after exit from the outer membrane of B. **pertussis**.

L30 ANSWER 19 OF 30 MEDLINE DUPLICATE 10
AN 94089352 MEDLINE
TI Acellular and whole-cell **pertussis vaccines** as booster doses: a multicenter study.
AU Englund J A; Decker M D; Edwards K M; Pichichero M E; Steinhoff M C; Anderson E L
CS Dept of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77096..
NC NO1-AI72629 (NIAID)
NO1-AI62515 (NIAID)
NO1-AI05049 (NIAID)
+
SO PEDIATRICS, (1994 Jan) 93 (1) 37-43.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)

Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9403
AB OBJECTIVE. To compare the safety and immunogenicity of a variety of acellular (AC) and whole-cell (WC) **pertussis** **vaccines** combined with diphtheria and tetanus **toxoids**. METHODS. Standard enrollment and reaction forms were used at five sites, and serologic evaluation was performed at a single site. Nine AC (Massachusetts Public Health Laboratories, Biocine Sclavo recombinant **pertussis toxoid** [PT], Connaught/BIKEN, Lederle three-component, Biocine Sclavo recombinant three-component, SmithKline Beecham three-component, Porton three-component, Takeda-Wyeth, and Connaught multicomponent), and three WC (Connaught Laboratories, Lederle Laboratories, and Massachusetts Public Health Laboratories) were studied. All AC contained varying concentrations of PT; some **vaccines** also contained filamentous **hemagglutinin** (FHA), **pertactin**, and/or **agglutinogens**. RESULTS. Two hundred forty children, aged 16 to 21 months and 4 to 6 years, were enrolled at five sites. Significantly less fever, redness, swelling, pain, limp, and use of pain medication were noted following AC compared with WC. Significant increases in antibody to PT were seen following all **vaccines**. Significant rises in FHA antibody were seen following all WC and the seven AC that contained FHA. Postbooster PT antibody levels were similar among the AC groups, regardless of the amount of PT administered (between 3.5 and 25 micrograms per dose). The dose of FHA did not affect PT antibody response. Infants primed with WC who were boosted with a monocomponent PT **vaccine** did not manifest a significant antibody response to FHA. CONCLUSION. The rate of adverse reactions was not a function of the number of antigens or the antigen quantity in the acellular **vaccines**, and antibody responses following AC were similar or better than antibody responses following WC. These results support the further evaluation of these **vaccines** in a larger National Institute of Allergy and Infectious Diseases-sponsored study in infants.

L30 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1993:145476 HCAPLUS
DN 118:145476
TI Bordetella **pertussis** and Bordetella parapertussis: Two immunologically distinct species
AU Khelef, Nadia; Danve, Bernard; Quentin-Millet, Marie Jose; Guiso, Nicole
CS Unite Bacteriol. Mol. Med., Inst. Pasteur, Paris, 75724, Fr.
SO Infect. Immun. (1993), 61(2), 486-90
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB The pathogens B. **pertussis** and B. parapertussis are closely related species. Both are responsible for outbreaks of whooping cough in humans and produce similar virulence factors, with the exception of **pertussis toxin**, specific to B. **pertussis**. Current **pertussis** whole-cell **vaccine** will soon be replaced by acellular **vaccines** contg. major adhesins (filamentous **hemagglutinin** and

pertactin) and major **toxin** (**pertussis toxin**). All of these factors are antigens that stimulate a protective immune response in the murine respiratory model and in clin. assays. The present study examd. the protective efficacies of these factors, and that of adenylate cyclase-hemolysin, another B. **pertussis toxin**, against B. parapertussis infection in a murine respiratory model. As expected, **pertussis toxin** did not protect against B. parapertussis infection, since this bacterium did not express this protein, but the surprising result was that none of the other factors were protective against B. parapertussis infection. Furthermore, B. parapertussis adenylate cyclase-hemolysin, although it protected against B. parapertussis infection, did not protect against B. **pertussis** infection. Despite a high degree of homol. between both B. **pertussis** and B. parapertussis species, no cross-protection was obsd. These results outline the fact that, as in other gram-neg. bacteria, Bordetella surface proteins vary immunol.

L30 ANSWER 21 OF 30 MEDLINE
AN 93227700 MEDLINE
TI Proliferative responses to purified and fractionated Bordetella **pertussis** antigens in mice immunized with whole-cell **pertussis vaccine**.
AU Petersen J W; Andersen P; Ibsen P H; Capiau C; Wachmann C H; Haslov K; Heron I
CS Bacterial Vaccine Department, Statens Seruminstitut, Copenhagen, Denmark..
SO VACCINE, (1993) 11 (4) 463-72.
Journal code: X6O. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9307
AB The specificity of the cell-mediated immune response to Bordetella **pertussis** following immunization of C57B1 mice with a whole-cell **pertussis vaccine** was assessed in a proliferation assay. A proliferative response of lymph node lymphocytes to the filamentous **haemagglutinin**, the 69 kDa outer membrane protein and the **agglutinogens** 2 and 3 was demonstrated. The proliferative cells were T cells of the CD4+ phenotype. In addition, several as yet uncharacterized antigens expressed by B. **pertussis** were shown to induce a proliferative response, also mediated by T cells of the CD4+ phenotype. Although a range of different immunization schedules and preparations of **pertussis toxin** were used, no specific proliferative responses to **pertussis toxin**, which is regarded as a protective antigen of major importance from B. **pertussis**, were found.

L30 ANSWER 22 OF 30 MEDLINE
AN 93190593 MEDLINE
TI Quantification of **pertussis toxin**, filamentous **haemagglutinin**, 69 kDa outer membrane protein, **agglutinogens** 2 and 3 and lipopolysaccharide in the Danish whole-cell **pertussis vaccine**.
AU Ibsen P H; Petersen J W; Heron I
CS Bacterial Vaccine Department, Statens Seruminstitut, Copenhagen,

Denmark..
SO VACCINE, (1993) 11 (3) 318-22.
Journal code: X6O. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9306
AB The amounts of **pertussis toxin** (PT), filamentous **haemagglutinin** (FHA), 69 kDa outer membrane protein (69 kDa OMP) and **agglutinogens** (AGG) 2 and 3 in extracts from the Danish whole-cell **pertussis vaccine** were studied in quantitative capture ELISA. With the exception of PT, the most effective extraction of these antigens was by heating the bacteria at 60 degrees C for 30 min in 2 M urea followed by sonication for 45 s. Extraction by 1 M sodium chloride prior to sonication resulted in higher levels of antigenic and biologically active PT. On average, a single human dose of **pertussis vaccine** (approximately 16 opacity units) was found to contain 5520 ng FHA, 63 ng PT, 1061 ng 69 kDa OMP, 397 ng AGG 2, 534 ng AGG 3 and 4840 ng lipopolysaccharide (LPS). The antigen content of one dose of the Danish **pertussis vaccine** appears to be low compared with the amounts found in the acellular **vaccines** currently in use. These findings may have important implications for the evaluation of the protective substances and the immunogenicity of whole-cell as opposed to acellular **pertussis vaccines**.

L30 ANSWER 23 OF 30 MEDLINE DUPLICATE 11
AN 93056720 MEDLINE
TI Controlled study of a new five-component acellular **pertussis vaccine** in adults and young children.
AU Englund J A; Glezen W P; Barreto L
CS Department of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77030..
SO JOURNAL OF INFECTIOUS DISEASES, (1992 Dec) 166 (6) 1436-41.
Journal code: IH3. ISSN: 0022-1899.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9302
AB A new five-component acellular **pertussis** (AP) **vaccine** containing 10 micrograms of **pertussis toxoid**, 5 micrograms of filamentous **hemagglutinin**, 5 micrograms of combined **agglutinogens** 2 and 3, and 3 micrograms of **pertactin** was evaluated in adults and young children. AP **vaccine** was compared with saline placebo in 31 adults, and AP **vaccine** combined with diphtheria and tetanus **toxoids** (ADTP) was compared with whole cell DTP in 41 children, ages 16-20 months, who had received whole cell DTP during infancy. AP was mildly to moderately reactogenic in adults, with pain noted within 72 h and 5-8 days after immunization. ADTP was less reactogenic than DTP in children, with significantly decreased pain, redness, irritability, and fever and less use of acetaminophen reported. No late reactions were observed in any

child. The multicomponent ADTP was immunogenic, with four-fold or greater antibody rises to at least four **pertussis** antibody assays in all 15 immunized adults. **Pertussis**-specific antibody responses in children who received ADTP and DTP were similar. The multicomponent ADTP **vaccine** is currently being studied in a National Institute of Allergy and Infectious Diseases-sponsored efficacy study in Sweden.

L30 ANSWER 24 OF 30 MEDLINE DUPLICATE 12
AN 93035111 MEDLINE
TI Immunogenicity and reactogenicity of Takeda acellular **pertussis**-component diphtheria-tetanus-**pertussis** **vaccine** in 2- and 3-month-old children in Japan.
AU Kamiya H; Nii R; Matsuda T; Yasuda N; Christenson P D; Cherry J D
CS Mie National Hospital, Tsu, Japan.
SO AMERICAN JOURNAL OF DISEASES OF CHILDREN, (1992 Oct) 146 (10) 1141-7.
Journal code: 3GS. ISSN: 0002-922X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9301
AB OBJECTIVE--To compare the reactogenicity and immune response to the Takeda acellular **pertussis**-component diphtheria-tetanus-**pertussis** (APDT) **vaccine** in children when immunization commenced at 2 months (group A) vs 3 months (group B) of age. DESIGN--Longitudinal, nonblinded, comparative study. SETTING--Pediatric well-child clinics. PARTICIPANTS--Healthy 50- to 98-day-old infants. RESULTS--Good antibody responses to lymphocytosis-promoting factor, filamentous **hemagglutinin**, **agglutinogens**, and **pertactin** occurred in both age groups after both the third and fourth **vaccine** doses. Both young age and transplacentally acquired maternal antibody independently and together have a suppressive effect on the response to the four antigens in this APDT **vaccine**. However, these effects appear to be minor. **Vaccine** reactions were mild; group A children had slightly but not significantly higher rates than group B children. CONCLUSION--The present US diphtheria and tetanus **toxoids** and **pertussis** **vaccine** immunization schedule should also be satisfactory with this acellular **pertussis** component **vaccine**.

L30 ANSWER 25 OF 30 MEDLINE DUPLICATE 13
AN 93110972 MEDLINE
TI Progress towards the development of new **vaccines** against whooping cough.
AU Rappuoli R; Podda A; Pizza M; Covacci A; Bartoloni A; de Magistris M T; Nencioni L
CS Immunobiology Research Institute, Siena, Italy.
SO VACCINE, (1992) 10 (14) 1027-32. Ref: 48
Journal code: X60. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9303

AB Acellular **vaccines** against whooping cough are in the final stage of clinical testing and are likely to become available for mass immunization in the near future. Over a dozen **vaccines** of similar composition have been developed by **vaccine** companies and research laboratories; all of them contain a detoxified form of **pertussis toxin** (PT) that may be present alone or combined with one or more other non-**toxic** proteins, such as filamentous **haemagglutinin** (FHA), **pertactin** (69 kDa), and the **agglutinogens** (AGG). Most of the **vaccines** contain a PT that has been inactivated by chemical treatment, a process that reduces the immunogenicity of the molecule and may not completely eliminate the risk of reversion to **toxicity**. To avoid these problems, we have constructed by genetic manipulation a mutant of Bordetella **pertussis** that produces a non-**toxic** form of PT. This molecule (PT-9K/129G) contains two amino acid substitutions in the S1 subunit (Arg9-->Lys and Glu129-->Gly) which abolish the enzymatic activity of the S1 subunit and all the **toxic** properties of PT, without changing the immunological properties of the wild-type **toxin**. Following extensive preclinical studies, which have shown that PT-9K/129G is safe and more antigenic than the **toxin** treated with chemical agents, this molecule was tested for safety and immunogenicity in adult volunteers, 18-month-old children and 2-month-old infants. The molecule has been tested alone, combined with FHA and **pertactin** and also combined with diphtheria and tetanus **toxoids**. (ABSTRACT TRUNCATED AT 250 WORDS)

L30 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1993:647407 HCAPLUS
DN 119:247407
TI Recent advances in the development of **pertussis vaccines**
AU Brennan, Michael J.; Burns, Drusilla L.; Meade, Bruce D.; Shahin, Roberta D.; Manclark, Charles R.
CS Cent. Biol. Eval. Res., FDA, Bethesda, MD, USA
SO Biotechnol. Ser. (1992), 20(Vaccines: New Approaches to Immunological Problems), 23-52
CODEN: BTGYDD; ISSN: 0740-7378
DT Journal; General Review
LA English
AB A review, with 206 refs., discussing Bordetella **pertussis toxins** and surface proteins as **vaccine** candidates and clin. studies of acellular **pertussis vaccines**.

L30 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1991:654329 HCAPLUS
DN 115:254329
TI Purification of **pertactin**, a **pertussis** outer membrane protein, for **vaccine**
IN Jackson, Gail; Fahim, Raafat; Tan, Larry; Chong, Pele; Vose, John; Klein, Michel
PA Connaught Laboratories Ltd., Can.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
PI WO 9115505 A1 911017
DS W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

AI WO 91-CA110 910403
PRAI GB 90-7657 900404
DT Patent
LA English
AB **Pertactin** (I) (formerly 69 kilodalton protein) is recovered in a stable biol. pure form having no detectable adenylate cyclase activity from broth from Bordetella **pertussis** fermn., as well as from the cells. The broth is processed to selectively remove **pertussis toxin** (PT) and filamentous **hemagglutinin** (FHA), I is pptd. by (NH4)2SO4, the ppt. is dissolved in pH 6.0-8.5 buffer, and the soln. is chromatographed on hydroxylapatite and Q-Sepharose before final ultrafiltration. Cells are extd. with urea, and the ext. is ultrafiltered and diafiltered. I is pptd. from the ext., and the ppt. is processed as above. In a variation, the broth is contacted with (NH4)2SO4 to ppt. I and PT and FHA, the ppt. is dissolved, and the PT and FHA are selectively removed before chromatog. of the soln. The obtained protein is useful for a component **vaccine** against whooping cough. The immunogenicity and stability of the purified I are described.

L30 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 1997 ACS
AN 1991:672712 HCAPLUS
DN 115:272712
TI The use of autologous promoters to express genes in Bordetella
IN Loosmore, Sheena; Zealey, Gavin; Yacoob, Reza Khayyam; Klein, Michel
PA Connaught Laboratories Ltd., Can.
SO Eur. Pat. Appl., 17 pp.
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AI EP 91-303320 910416
PRAI GB 90-8746 900418
DT Patent
LA English
AB A method for modulating the levels of expression of genes for antigens of Bordetella involved in the virulence reaction is described. The method puts these genes under the control of promoters from Bordetella virulence genes that are also controlled by the Bvq (Bordetella virulence regulating gene) function. Antigens or recombinant cells produced using the above method can be used as component or whole cell **vaccines**, resp. (no data). The promoters and coding regions of the genes for filamentous **hemagglutinin**, **pertactin**, and **pertussis toxin** were used. The expression of the **pertussis toxin** operon from the filamentous **hemagglutinin** gene promoter resulted in accumulation of **toxin** at a rate comparable to that found when the **toxin** operon is expressed from its own promoter. When the filamentous **hemagglutinin** gene was expressed from the weaker **pertussis toxin** operon promoter the yields of **hemagglutinin** were about half those of controls.

L30 ANSWER 29 OF 30 MEDLINE
AN 92157866 MEDLINE
TI Construction and characterization of Bordetella **pertussis** mutants lacking the vir-regulated P.69 outer membrane protein.
AU Roberts M; Fairweather N F; Leininger E; Pickard D; Hewlett E L; Robinson A; Hayward C; Dougan G; Charles I G

CS Department of Molecular Biology, Wellcome Biotech, Beckenham, Kent, UK..
SO MOLECULAR MICROBIOLOGY, (1991 Jun) 5 (6) 1393-404.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9205
AB The Bordetella **pertussis** P.69 protein is an immunogen with **vaccine** potential. The role of this protein in pathogenesis is unclear; it has been associated with the **toxic** adenylate cyclase and adhesion to eukaryotic cells. For further analysis of the role of P.69 in the biology of B. **pertussis**, we have constructed strains which specifically lack P.69. The cloned P.69 (prn) gene of B. **pertussis** was insertionally inactivated with a kanamycin-resistance cassette. This inactivated gene was used to construct P.69- mutants of B. **pertussis** by allelic exchange using plasmid pRTP1. B. **pertussis** P.69- strains produced normal levels of other vir-regulated factors, including adenylate cyclase. The serotype of B. **pertussis**, determined by Eldering and Preston typing sera and monoclonal antibodies, was also unaffected by the presence or absence of P.69. The ability of a prn mutant to adhere to and invade HEp2 cells was not significantly different from that of its parent strain. A strain containing a mutation in fhaB was significantly less adhesive and invasive than its parent, and a prn fhaB double mutant exhibited an even greater reduction in adhesiveness and invasiveness down to levels comparable with a Vir- strain. However, strains harbouring mutations in FHA and/or P.69 were able to colonize or multiply in the murine respiratory tract, although a Vir- strain was unable to survive and proliferate in the same infection model.

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AN 91:422885 BIOSIS
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TI **PERTUSSIS VACCINE** UPDATE.
AU CORBEL M J
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SO 162ND MEETING OF THE PATHOLOGICAL SOCIETY OF GREAT BRITAIN AND IRELAND, CAMBRIDGE, ENGLAND, UK, JANUARY 3-5, 1991. J MED MICROBIOL 34 (4). 1991. II. CODEN: JMMIAV ISSN: 0022-2615
DT Conference
LA English